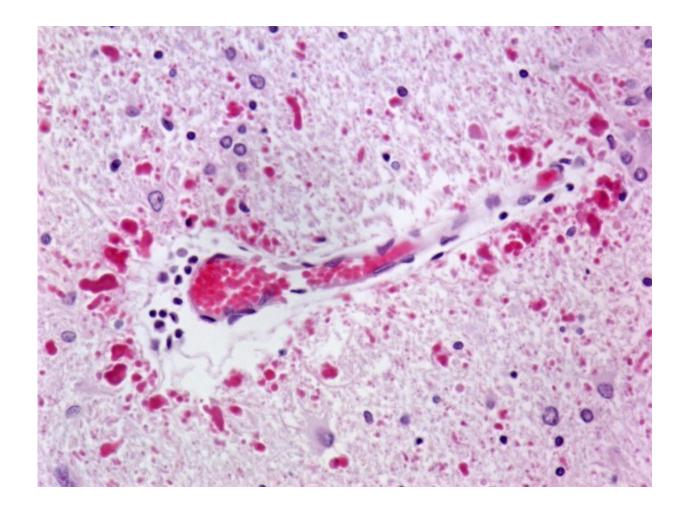


Tracing a path toward neuronal cell death

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Standard histology H&E staining of tissue from an eight-year-old Alexander disease patient. Rosenthal fibers -- the hallmark of the disease -- are shown in pink; nuclei are shown in blue. Credit: Liqun Wang, Feany lab

A fruit fly model of a rare, neurodegenerative disease is helping



researchers trace the series of steps that lead to neuronal cell death. Damage to astrocytes - star-shaped cells found in the brain and spinal cord - is found in many neurodegenerative conditions, but it's been unclear exactly what role astrocyte dysfunction plays in the development of disease.

Researchers at Brigham and Women's Hospital (BWH) have developed a genetic model that is yielding new insights into what happens when astrocytes go awry. The research team developed a fruit fly model of Alexander disease, a neurodegenerative disease that primarily affects astrocytes, and was able to narrow in on the molecular signals leading to neuronal cell death, identifying nitric oxide (NO) as a critical mediator. The team verified their results in a mouse model and also found evidence of activation of the same pathway in samples from patients with Alexander disease.

"We're excited to be contributing to a growing area of study of how astrocytes contribute to neurodegeneration, and to have uncovered a role for NO as a neuronal cell death signaling molecule," said corresponding author Mel B. Feany, MD, PhD, a senior pathologist in the BWH Department of Pathology. "Our findings define a potential mechanism for neuronal cell death in Alexander disease and possibly other neurodegenerative diseases with astrocyte dysfunction."

More information: Liqun Wang et al. Nitric oxide mediates glial-induced neurodegeneration in Alexander disease, *Nature Communications* (2015). DOI: 10.1038/NCOMMS9966

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